UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/764,016	01/23/2004	David Fikstad	23625.CON	8956

20551 7590 07/24/2008
THORPE NORTH & WESTERN, LLP.
P.O. Box 1219
SANDY, UT 84091-1219

EXAMINER	
ROYDS, LESLIE A	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
07/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/764,016	FIKSTAD ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-2,13-15,20-24,29-33,38-39,42-65* is/are pending in the application.

4a) Of the above claim(s) *44-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2,13-15,20-24,29-33,38-39,42-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-2, 13-15, 20-24, 29-33, 38-39 and 42-65 are presented for examination.

Applicant's Amendment filed February 28, 2008 has been received and entered into the present application.

Claims 1-2, 13-15, 20-24, 29-33, 38-39 and 42-65 remain pending. Claims 1-2, 13-15, 20-24, 29-33, 38-39 and 42-43 remain under examination. Claims 44-65 remain withdrawn from consideration pursuant to 37 C.F.R. 1.142(b). Claims 1 and 32-33 are amended and claims 16-19 are cancelled.

Applicant's arguments, filed February 28, 2008 have been fully considered. Rejections and objections not reiterated are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 13-15, 20-24, 29, 32-33, 38 and 42-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Amselem et al. (U.S. Patent No. 5,891,469; 1999), already of record, for the reasons of record set forth at pages 7-9 of the previous Office Action dated September 7, 2007, of which said reasons are herein incorporated by reference.

Newly amended claims 1 and 32-33 now require that the instantly claimed pharmaceutical composition (or oral dosage form as in instant claim 32 or a solid oral dosage form as in instant claim 33) comprising a therapeutically effective amount of a drug, a solubilizer and a release modulator is formulated to release the drug over an extended period of time, said extended period of time being

between 2 and 24 hours. Such claims remain properly included in the instant rejection because Amselem demonstrates that pharmaceutical compositions prepared according to the disclosure of the reference are capable of release of the active drug over 120 minutes, which is equivalent to Applicant's "extended period of time" of 2 hours as instantly claimed (see, e.g., instant claims 1 and 32-33). Please see, e.g., Figure 1 of Amselem, which measured the percentage release of the active therapeutic agent (i.e., dexanabinol) over 120 minutes using various formulations prepared according to the invention as disclosed. Note also, that Applicant's term "extended period of time" as defined in the instant specification at p.4, l.17-19 does not require any particular quantity or amount of active agent to be released over the instantly claimed period of time. Accordingly, since Amselem clearly demonstrates that exemplary compositions prepared in accordance with the invention as disclosed are formulated such that they are capable of release of the active therapeutic agent over at least 120 minutes (i.e., 2 hours; see, e.g., Figure 1), the prior art disclosure anticipates the instantly claimed invention.

Response to Applicant's Arguments

Applicant traverses the instant rejection, stating that each of the independent claims has been amended to require that the drug is released over an extended period of time of 2-24 hours, which is allegedly not taught by Amselem. Applicant accordingly requests that the rejection be withdrawn.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

For the reasons presented *supra*, Amselem, contrary to Applicant's allegations, does, in fact, teach release of the active drug over at least 120 minutes (i.e., 2 hours), which meets Applicant's instantly claimed requirement that the pharmaceutical composition be formulated such that the drug is released over an extended period of time of 2-24 hours. Accordingly, Amselem continues to anticipate instant claims 1, 13-15, 20-24, 29, 32-33, 38 and 42-43.

For these reasons set forth *supra*, and those previously made of record at pages 7-9 of the Office Action dated September 7, 2007, rejection of claims 1, 13-15, 20-24, 29, 32-33, 38 and 42-43 remains proper and is **maintained**.

Claim Rejections - 35 USC § 103 (New Grounds of Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 13-15, 20-24, 29-33, 38 and 42-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amselem et al. (U.S. Patent No. 5,891,469; 1999) in view of The Merck Index (Eleventh Edition, Monograph 3924; 1989, p.624-625) and The Merck Index (Twelfth Edition, Monograph 504; 1996, p.84).

Amselem teaches pharmaceutical compositions capable of increasing the oral bioavailability of a lipophilic substance (col.5, l.40-50), comprising: (1) a lipophilic substance that possesses low water solubility and poor oral bioavailability (col.1, l.21-22), such as lipophilic substances that have a water solubility of less than 50 μg/ml (col.5, l.43-47), e.g., cannabinoids (col.5, l.44), which have aqueous

solubility of a few micrograms or less (i.e., meets Applicant's limitation directed to solubility of 25 μg/ml or less as stated in claim 15), (2) the surfactant alpha-tocopherol polyethylene glycol succinate (also meets Applicant's limitation directed to "tocopherol succinate", see, e.g., present claims 42-43), usually with a mean molecular weight of 1000 (col.5, l.49-66), and further (3) at least one dispersion adjuvant, such as tocopherol acetate, polyvinylpyrrolidone, a medium or long chain triglyceride and/or polyethylene glycol (col.6, l.23-26 and col.6, l.58-66). Amselem also teaches that the disclosed composition may be administered in a therapeutically effective amount to a mammal in need of such a substance (see claim 19; col.14), wherein the substance may be in a gelatin capsule or tablet unit dosage form (see claims 9-10; col.14) and may also comprise any suitable nontoxic carrier or diluent powder or additive (col.7, l.4-15). Amselem further teaches that the lipophilic substance is present from 0.01-50% of the total solid weight of the composition, the surfactant TPGS is present from 5-65% of the total solid weight of the composition and the dispersion adjuvant is present from 5-75% of the total solid weight of the composition (col.6, l.37-57). Still further, Amselem demonstrates that pharmaceutical compositions prepared according to the disclosure of the reference are capable of release of the active drug over 120 minutes, which is equivalent to Applicant's "extended period of time" of 2 hours as instantly claimed (see, e.g., instant claims 1 and 32-33). Please see, e.g., Figure 1 of Amselem, which measured the percentage release of the active therapeutic agent (i.e., dexanabinol) over 120 minutes using various formulations prepared in accordance with the invention as disclosed.

The teaching of tocopherol polyethyleneglycol (PEG) succinate in Amselem, especially tocopherol polyethyleneglycol 1000 succinate, as the surfactant component of the disclosed pharmaceutical composition places the use of either the racemic or either enantiomeric form (d- or l-) of tocopherol PEF succinate clearly within the possession of the public. Furthermore, though Amselem et al. does not expressly recognize the "release modulating" properties of the, e.g., tocopherol PEG succinate, tocopherol acetate, polyvinylpyrrolidone, or medium or long chain triglyceride, the very

teaching of the identical chemical entity in overlapping amounts clearly indicates that whatever release modulating properties that Applicant has attributed to either of these compounds are necessarily present, absent factual evidence to the contrary, since chemical compounds cannot have mutually exclusive properties. Please reference MPEP §2112.01.

With regard to present claims 20-23, directed to the solubilizer increasing the solubility of the drug by at least 25% compared to the intrinsic aqueous solubility of the drug (claim 20) or the synchronized release of the drug and solubilizer with a correlation coefficient of greater than 0.80 or 0.90 or 0.95 (claims 21-23), such correlation values are, absent factual evidence to the contrary, present in the reference because Amselem et al. teaches identical pharmaceutical formulations containing elements identical to, and capable of performing the same functions as, those elements presently claimed in the instant invention. In other words, the fact that Amselem et al. teaches identical components in what, on its face, appears to be an identical configuration to that presently claimed, is clearly indicative of the fact that any release characteristics attributed to such a composition would be necessarily present in the prior art of Amselem et al., absent factual evidence to the contrary. Please see MPEP §2112.01[R-3] ("Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ 2d 1655, 1658 (Fed. Cir. 1990)).

Lastly, while the limitation of "wherein the aqueous solubility of the drug is dependent on pH" in present claim 29 has been considered, such a limitation fails to further limit the composition of parent claim 1 because it fails to impart any physical or material property to the composition that is not already present in the claim from which it depends.

Amselem et al. fails to teach the specific therapeutic drugs instantly claimed (such as, *inter alia*, fenofibrate as in instant claim 2 or, *inter alia*, amiodarone as in instant claim 31).

In view of the fact that Amselem et al. teaches the disclosed pharmaceutical compositions for formulating any of a variety of lipophilic substances, i.e., those with low water solubility and poor oral bioavailability, one of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to use such a delivery preparation for the formulation of other highly hydrophobic drugs (i.e., those with low water solubility and, thus, poor bioavailability), such as fenofibrate or amiodarone, because, as The Merck Index teaches, the antihyperlipoproteinemic agent fenofibrate was well known in the art to be practically insoluble in water (see Monograph 3924) and the antiarrhythmic agent amiodarone was well known in the art to be only very slightly soluble in water (see Monograph 504). Accordingly, in view of the extensive hydrophobicity of both the compounds taught by Amselem et al. and fenofibrate and/or amiodarone, the skilled artisan would have had a reasonable expectation of success in effectively solubilizing fenofibrate and/or amiodarone in the delivery vehicle disclosed by Amselem et al. because of the demonstrated success in effectively solubilizing the exemplary hydrophobic agents (i.e., dexanabinol, CoQ10, etc.) of the reference into such a formulation. Further, such a person would have been motivated to do so in order to enable effective dosing of fenofibrate with concomitant enhancement of resorption and bioavailability levels, reduced variability in resorption and bioavailability levels and also a concomitant reduction in the amount required to achieve effective dosing.

Claims 1, 13-15, 20-24, 29, 32-33, 38-39 and 42-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amselem et al. (U.S. Patent No. 5,891,469; 1999) in view of Banker (U.S. Patent No. 3,097,144; 1963), each already of record.

Amselem et al. as applied above.

Amselem et al. fails to teach the specific use of a polyvinylpyrrolidone-vinyl acetate copolymer as the polyvinylpyrrolidone copolymer of the disclosed invention (claim 39).

Banker teaches heat-cured polymeric film coatings for medicinal compositions that contain polyvinylpyrrolidone copolymers (title), such as, e.g., a polyvinylpyrrolidone-vinyl acetate copolymer (col.2, l.20-27), that impart protection from moisture, reduce wear and chipping during handling and shipping an disguise unpleasant tastes (col.1, l.25-29) in solid medicinal dosage forms, such as tablets (col.1, l.23-25).

One of ordinary skill in the art would have found it *prima facie* obvious to apply the technique of coating the tablet formulation of Amselem et al. with the heat-cured polymeric film coating containing, e.g., polyvinylpyrrolidone-vinyl acetate copolymer, to improve the tablet formulation for the predictable results of imparting protection from moisture, enhancing integrity of the tablet by reducing wear and chipping that would have reasonably occurred during handling and shipping of the tablet formulations and also to enhance the aesthetics and palatability of the tablet by, for example, disguising unpleasant tastes.

Conclusion

Rejection of claims 1-2, 13-15, 20-24, 29-33, 38-39 and 42-43 is proper.

Claims 44-65 remain **withdrawn** from consideration pursuant to 37 C.F.R. 1.1.42(b).

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
Patent Examiner, Art Unit 1614

July 16, 2008

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614